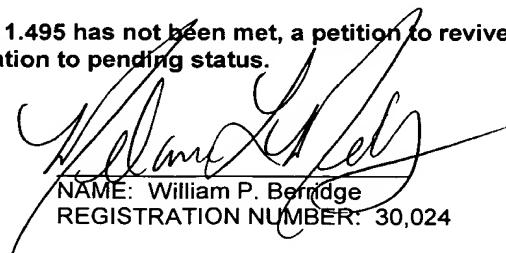
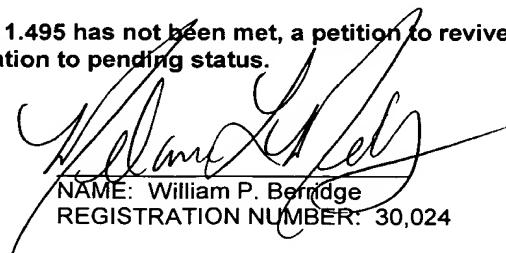
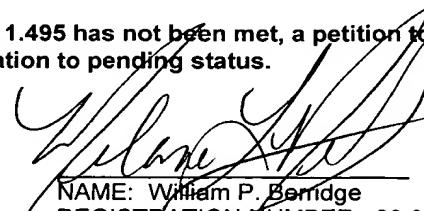
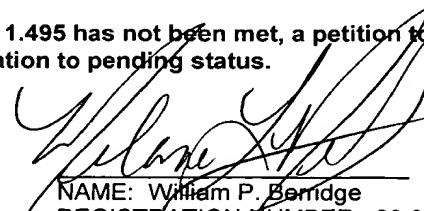


(1390 REV. 5-93) US DEPT. OF COMMERCE PATENT & TRADEMARK OFFICE TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NUMBER 111380 #11 U.S. APPLICATION NO. (if known, sec 37 C.F.R.1.5) 09/980,777
INTERNATIONAL APPLICATION NO. PCT/FR00/01728	INTERNATIONAL FILING DATE June 21, 2000	PRIORITY DATE CLAIMED June 21, 1999
TITLE OF INVENTION SEARCH METHOD FOR RESISTANCE TO ANTI-PROTEASES OF A STRAIN OF THE HIV 2 VIRUS FROM A BIOLOGICAL SAMPLE TAKEN FROM A PATIENT		
APPLICANT(S) FOR DO/EO/US Jean-Noel TELLES et al.		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> 1. <input type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input checked="" type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). 4. <input type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. 5. <input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ul style="list-style-type: none"> a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US) 6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)). 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ul style="list-style-type: none"> a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input checked="" type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)). 		
Items 11. to 16. below concern other document(s) or information included:		
<ol style="list-style-type: none"> 11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. <ul style="list-style-type: none"> <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> Entitlement to small entity status is hereby asserted. 16. <input checked="" type="checkbox"/> Other items or information: Response to Notification of Missing Requirements 		

U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) 09/980,777	INTERNATIONAL APPLICATION NO. PCT/FR00/01728	ATTORNEY'S DOCKET NUMBER 111380		
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS		
Basic National fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO\$890.00 International preliminary examination fee paid to USPTO (37 CFR 1.482)\$710.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2))\$740.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO\$1,040.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)\$ 100.00		PTO USE ONLY		
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$		
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$130.00		
Claims	Number Filed	Number Extra	Rate	
Total Claims			X \$ 18.00	\$
Independent Claims			X \$ 84.00	\$
Multiple dependent claim(s)(if applicable)			+ \$280.00	\$
TOTAL OF ABOVE CALCULATIONS =		\$130.00		
Reduction by 1/2 for filing by small entity, if applicable.		-	\$	
		SUBTOTAL =	\$130.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 month from the earliest claimed priority date (37 CFR 1.492(f)).		\$130.00		
		+		
TOTAL NATIONAL FEE =		\$260.00		
02/25/2002 MNGUYEN 00000072 09980777 01 FC:154 130.00 OP 02 FC:156 130.00 OP		Amount to be refunded	\$	
		Charged	\$	
a. <input checked="" type="checkbox"/>	Check No. <u>127941</u> in the amount of <u>\$260.00</u> to cover the above fees is enclosed.			
b. <input type="checkbox"/>	Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.			
c. <input checked="" type="checkbox"/>	The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. <u>15-0461</u> . A duplicate copy of this sheet is enclosed.			
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.				
SEND ALL CORRESPONDENCE TO: OLIFF & BERRIDGE, PLC P.O. Box 19928 Alexandria, Virginia 22320				
 NAME: William P. Berridge REGISTRATION NUMBER: 30,024				
Date: <u>February 20, 2002</u>  NAME: Melanie L. Mealy REGISTRATION NUMBER: 40,085				

Rec'd PTO/PTO 20 FEB 2002

U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) 09/980,777	INTERNATIONAL APPLICATION NO. PCT/FR00/01728	ATTORNEY'S DOCKET NUMBER 111380		
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS		
Basic National fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO\$890.00 International preliminary examination fee paid to USPTO (37 CFR 1.482)\$710.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2))\$740.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO\$1,040.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)\$ 100.00		PTO USE ONLY		
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$		
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$130.00		
Claims	Number Filed	Number Extra	Rate	
Total Claims			X \$ 18.00	\$
Independent Claims			X \$ 84.00	\$
Multiple dependent claim(s)(if applicable)			+ \$280.00	\$
TOTAL OF ABOVE CALCULATIONS =		\$130.00		
Reduction by 1/2 for filing by small entity, if applicable.		-	\$	
		SUBTOTAL =	\$130.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 month from the earliest claimed priority date (37 CFR 1.492(f)).		+	\$130.00	
TOTAL NATIONAL FEE =		\$260.00		
		Amount to be refunded	\$	
		Charged	\$	
a. <input checked="" type="checkbox"/>	Check No. <u>127941</u> in the amount of <u>\$260.00</u> to cover the above fees is enclosed.			
b. <input type="checkbox"/>	Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.			
c. <input checked="" type="checkbox"/>	The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. <u>15-0461</u> . A duplicate copy of this sheet is enclosed.			
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.				
SEND ALL CORRESPONDENCE TO: OLIFF & BERRIDGE, PLC P.O. Box 19928 Alexandria, Virginia 22320				
 NAME: William P. Berridge REGISTRATION NUMBER: 30,024				
Date: <u>February 20, 2002</u>  NAME: Melanie L. Mealy REGISTRATION NUMBER: 40,085				

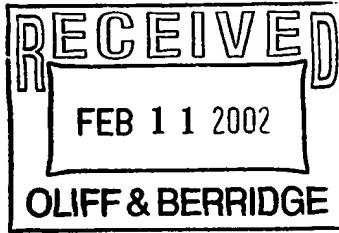


UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents, U.S.P.T.O.
United States Patent and Trademark Office
Washington, D.C. 20591-0000
www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATL.Y DOCKET NO
09/980,777	Jean-Noel Telles	111380

Oliff & Berridge
PO Box 19928
Alexandria, VA 22320



Date Mailed: 02/05/2002

INTERNATIONAL APPLICATION NO

PCT/FR00/01728

I.A. FILING DATE

03/21/2000

PRIORITY DATE

06/21/1999

CONFIRMATION NO. 8868
371 FORMALITIES LETTER



OC000Q0007413635

DUE DATE APR 05 2002

Missing
Parts

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as an Elected Office (37 CFR 1.495):

- U.S. Basic National Fees
- Priority Document
- Biochemical Sequence Listing
- Copy of IPE Report
- Copy of references cited in ISR
- Copy of the International Application
- Copy of the International Search Report
- Information Disclosure Statements
- Request for Immediate Examination

DOCKETED
 By PPD on 2/11/2002
 and
 By MM on 2/11/2002
 Oliff & Berridge

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Translation of the application into English.
- Processing fee for providing the translation of the application and/or the Annexes later than the appropriate 30 months from the priority date (37 CFR 1.492(f)).
- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.
- \$130 Surcharge for providing the oath or declaration later than the appropriate 30 months months from the priority date (37 CFR 1.492(e)) is required.

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTH FROM THE DATE OF THIS NOTICE OR BY 22 or 32 MONTHS (where 37 CFR 1.495 applies) FROM THE PRIORITY DATE FOR

THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

The following items **MUST** be furnished within the period set forth below:

- The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825 for the following reason(s):
 - A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).
 - A copy of the "Sequence Listing" in computer readable form has been submitted. The content of the computer readable form, however, does not comply with the requirements of 37 CFR 1.822 and/or 1.832, as indicated on the attached marked-up copy of the "Raw Sequence Listing."
 - **APPLICANT MUST PROVIDE:**
 - An initial or substitute computer readable form (CRF) of the "Sequence Listing."
 - An initial or substitute paper copy or compact disc of the "Sequence Listing," as well as an amendment directing its entry into the specification.
 - A statement that the contents of the paper or compact disc and the computer readable form are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d).
- For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:
 - For Rules Interpretation, call (703) 308-4216
 - To Purchase PatentIn Software, call (703) 306-2600
 - For PatentIn Software Program Help, call (703) 306-4119 or e-mail at patin21help@uspto.gov or patin3help@uspto.gov

SUMMARY OF FEES DUE:

Total additional fees required for this application is **\$260** for a Large Entity:

- **\$130** Late oath or declaration Surcharge.
- **\$130** for English translation surcharge required.
- A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).
- A copy of the "Sequence Listing" in computer readable form has been submitted. The content of the computer readable form, however, does not comply with the requirements of 37 CFR 1.822 and/or 1.832, as indicated on the attached marked-up copy of the "Raw Sequence Listing."

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

BARBARA A CAMPBELL

Telephone: (703) 305-3631

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY DOCKET NO
09/980,777	PCT/FR00/01728	111380

FORM PCT/DO/EO/905 (371 Formalities Notice)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Jean-Noel TELLES et al.

Attn: PCT Branch

Application No. 09/980,777

Filed: February 20, 2002

Docket No.: 111380

For: SEARCH METHOD FOR RESISTANCE TO ANTI-PROTEASES OF A STRAIN
OF THE HIV-2 VIRUS FROM A BIOLOGICAL SAMPLE TAKEN FROM A
PATIENT

RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS
UNDER 35 U.S.C 371 IN THE UNITED STATES DESIGNATED/
ELECTED OFFICE (DO/EO/US) WITH DECLARATION,
TRANSLATION AND SEQUENCE LISTING

Director of the U.S. Patent and Trademark Office
Washington, D.C. 20231

Sir:

In response to the Notification of Missing Requirements Under 35 U.S.C 371 in the United States Designated/Elected Office (DO/EO/US) (copy attached) mailed on February 5, 2002, submitted herewith is the executed Declaration of the inventors and, upon information and belief, an accurate translation of the application. Any specification attached to and referenced in the Declaration is a copy of the specification and any amendments thereto which were filed in the Office in order to obtain a filing date for the application.

(Column 1)	(Column 2)	(Column 3)	SMALL ENTITY	OTHER THAN A SMALL ENTITY
CLAIMS REMAINING AFTER TRANSLATION	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADD'L FEE
TOTAL CLAIMS	*14 MINUS	**20	=0	
INDEP CLAIMS	*2 MINUS	***3	=0	
<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEP. CLAIM			OR	
			OR	
			RATE	ADD'L FEE
			x 9	\$
			x 42	\$
			+140	\$
				\$

- * If the entry in Column 1 is less than the entry in Column 2, write "0" in Column 3.
- ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
- *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space.

The "Highest Number Previously Paid For" in this space (Total or Independent) is the highest number found from the equivalent box in Column 1 of a prior Amendment or the number of claims originally filed.

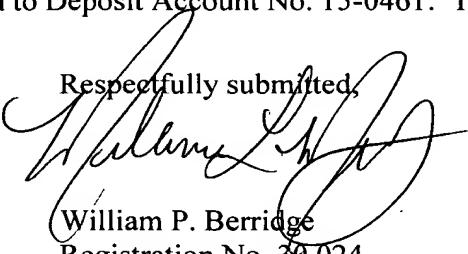
Attached is our Check No. 127941 for \$260.00 \$195.00 (entitlement to small entity status is asserted) for the fee under 37 C.F.R. §§ 1.492(e) and (f) and any excess claim fees noted above.

Also attached is a Preliminary Amendment forwarding identical paper and computer readable copies of the Sequence Listing as required by 37 CFR 1.821, 37 CFR 1.822 and/or 1.832.

Entry of these documents should complete all of the filing formalities and fully satisfy all requirements of the Notification of Missing Requirements. Accordingly, prompt issuance of a Notification of Acceptance and Official Filing Receipt, and prompt examination and allowance of this application are respectfully solicited.

The Director is hereby authorized to charge any additional fee (or credit any overpayment) associated with this communication to Deposit Account No. 15-0461. Two duplicate copies of this paper are attached.

Respectfully submitted,


William P. Berridge
Registration No. 30,024

Melanie L. Mealy
Registration No. 40,085

WPB:MLM/zmc

Attached:

Executed Declaration
English-language Translation
Preliminary Amendment
Paper Sequence Listing
Computer Readable Sequence Listing

Date: February 20, 2002

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461

PCT/PTO 20 FEB 2002

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Jean-Noel TELLES et al.

Attn: PCT Branch

Application No. 09/980,777

Filed: February 20, 2002

Docket No.: 111380

For: SEARCH METHOD FOR RESISTANCE TO ANTI-PROTEASES OF A STRAIN
OF THE HIV-2 VIRUS FROM A BIOLOGICAL SAMPLE TAKEN FROM A
PATIENT

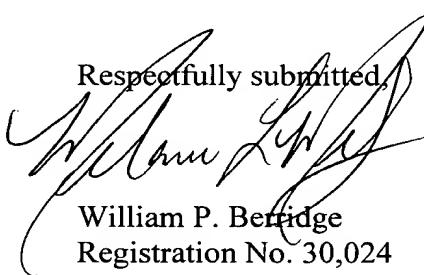
TRANSLATION OF THE ANNEXES TO THE
INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Director of the U.S. Patent and Trademark Office
Washington, D.C. 20231

Sir:

Attached hereto is a translation of the annexes to the International Preliminary Examination Report (Form PCT/IPEA/409). The attached translated pages 15 and 16 replace the original translated pages 15 and 16.

Respectfully submitted,


William P. Berridge
Registration No. 30,024

Melanie L. Mealy
Registration No. 40,085

WPB:MLM/zmc

Date: February 20, 2002

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

**DEPOSIT ACCOUNT USE
AUTHORIZATION**
Please grant any extension
necessary for entry;
Charge any fee due to our
Deposit Account No. 15-0461

6. Method according to Claim 1, wherein said test is carried out using sequencing techniques, according to known methods.

7. Nucleotide probe usable in the method according to any one of Claims 1 to 5, comprising, as a minimum sequence, a sequence chosen from the group comprised of:

CCA AGA ATA for a mutated form of position 45.

CCA AGA GTA for a mutated form of position 45.

CCT AGA ATA for a mutated form of position 45.

TTT ATG AAC for a mutated form of position 54.

TTT ATG AAT for a mutated form of position 54.

GAA GTA AAA for a mutated form of position 64.

GAA GTA GAA for a mutated form of position 64.

AAC CTC TTT for a mutated form of position 84.

ATT ATG ACA for a mutated form of position 90.

ATC ATG ACA for a mutated form of position 90,

possibly supplemented by the nucleotide sequence of an adjacent region of the gene of said protease, on either side of the minimum sequence,

(b) a nucleotide sequence equivalent to a sequence defined in (a), and

(c) a sequence complementary to a sequence defined in (a) or in (b).

8. Method for testing, in a biological sample from a patient infected by HIV-2 containing at least one HIV-2 viral strain, the resistance of the HIV-2 viral strain to treatment with an antiprotease agent, wherein, using known methods, the presence of at least one mutation in position 10 or 46 of the protein sequence of the protease of said viral strain is investigated, said mutation having previously been found to elicit said resistance, and wherein, if such a mutation is found, it is concluded that a viral strain resistant to said antiprotease agent is present in the patient in question.

9. Method according to Claim 8, wherein:

a) using known methods, the presence of at least one mutation at one of said positions of the protein sequence of the protease of said viral strain in a biological sample taken from a patient infected with HIV-2 is investigated,

b) of the mutations founds in a), those which, after cloning in an HIV-2 virus, do not prevent the virus clone obtained from multiplying in culture in the presence of said antiprotease drug are selected, and

c) if at least one mutation is selected at step b), it is concluded that resistance exists to the antiprotease drug referred to in b).

10. Method according to Claim 8, wherein the presence of at least one mutation chosen from the following mutations:

V 10 I, I 46 V, and I 82 M

in the protein sequence of the protease of said viral strain is investigated and in which said resistance is concluded to exist if said mutation or said mutations is or are present.

11. Method according to any of Claims 8 to 10, wherein, to detect a mutation of the protein sequence of the protease, a corresponding mutation is sought in the nucleotide sequence of the gene of said protease.

12. Method according to Claim 11, wherein said test is carried out using sequencing techniques, according to known methods.

13. Method according to Claim 11, wherein said test is carried out using hybridization techniques, according to known methods.

14. Nucleotide probe usable in the method according to Claim 13, comprising, as a minimum sequence, a sequence chosen from the group comprised of:

(a) CCA ATA GTC for a mutated form of position 10.

AAA GTA GTA for a mutated form of position 46.

CCA ATG AAC for a mutated form of position 82.

possibly supplemented by the nucleotide sequence of an adjacent region of the gene of said protease, on either side of the minimum sequence,

(b) a nucleotide sequence equivalent to a sequence defined in (a), and

(c) a sequence complementary to a sequence defined in (a) or in (b).